Ridom EpiMRSA

Version 3

User Guide

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1.Introduction

Overview

Staphylococcus aureus (*S. aureus*) is the cause of the most hospital-acquired infections worldwide. Thereby infections are particularly susceptible to being caused by Methicillin-resistant *S. aureus* (MRSA), for which there are only few, if any, possibilities of antibiotic therapy. It has been clearly demonstrated by various authors that Methicillin resistance is directly associated with increased mortality and morbidity with *S. aureus* infections. In the last 10 years an increase in the MRSA rate from 2% to approx. 25% was observed in Germany. In the Netherlands and Scandinavia a stable rate under 3% has been recorded for years. Particularly, for the Netherlands, adhering to a consequent "search and destroy" policy, MRSA felt off to very low rates and is now under control. In the Netherlands the main focus will be on isolating and controlling CA-MRSA, that are a possible danger for the open population outside hospitals. The main aim of the project is the creation of a network of the major health care providers in the region and the achieving of a lower MRSA rate, a reduction of the number of MRSA infections and thus a shorter stay in hospital as a result. A basic requirement for this is the active education of the region's population by the EUREGIO network. A transborder quality group from hospitals, public health authorities and laboratories is therefore planned over the course of three years. The network aims to consolidate those already locally established resources (e.g. laboratories, hygiene specialists, etc.) and will be coordinated by the two headquarters, Münster and Enschede, in order to organize the containment of MRSA more effectively.

The basis of all efforts for the fight against MRSA comprises

1. Rational antibiotic therapy in order to reduce the selective pressure
2. Prevention
    - Real implementation of the hygiene measures according to guidelines
    - Isolation of potential MRSA carriers
3. Surveillance
    - Early laboratory-diagnostic identification of carriers, in order to avoid nosocomial transmission as soon as possible
    - Molecular classification of the MRSA isolates in order to recognize transmission chains and to gain an overview of the dynamics of the spread and persistence in the patient
4. Therapy and decontamination of the infected and/or colonized persons during and after hospitalization
5. Education of the population as well as further training of personnel in the health care service

Cited from: http://www.mrsa-net.eu/

The Ridom EpiMRSA software is an integral part of the strategy for prevention, surveillance and decontamination of MRSA.

Software Features

Database

- The personal data (encrypted) and relevant epidemiological information can be stored locally in the database system incorporated in the EpiMRSA software.
- Information from the database can easily be exported in comma-separated, spreadsheet format. The same format can also be imported.
- The integrity of the database is checked regularly and the contents can be backed up to prevent data leakage.

Report Generator

- Reports can be created with various configurations using EpiMRSA.
- These reports are stored internally as read-only, tamper-proof and encrypted PDF files.
- MRSA NIS Reports and ÖGD Reports can be created for use in MRSA surveillance.

Spa-type up-to-date service

- EpiMRSA automatically searches for new spa-types on the SpaServer, and retrieves them.

Protection of Data Privacy

All personal data are saved encrypted in the database using a password based cipher with a 128bit key.

How to Contact Us

You can contact with requests for support:

- by email: support@ridom.de
- by the built-in support-dialog of EpiMRSA in the Help menu

2.Installing EpiMRSA

System Requirements

Hardware Requirements

- 1 GB RAM
- Hard disk with at least 200 MB available space (depending on database size)
- One free USB port for the hardware key (Dongle).

Hardware Key (Dongle)

EpiMRSA may be installed on different computers without registration- or activation-codes. However, the Ridom hardware key ("Dongle") that was delivered together with the software must be plugged to the computer when working with the EpiMRSA. The installation program includes a specific device driver made available by the manufacturer of the key device (WIBU Systems).

If the computer where EpiMRSA is installed has no accessible USB ports, it is possible to apply the hardware key to a server computer. The hardware key of the server computer can than be used by any other computer in the same local network. If this is needed, please contact support@ridom.de for further information.

Software Requirements

- Microsoft Windows 7 / Vista / XP / 2000
- Adobe Reader software must be installed to view or print PDF reports

Installing Instructions

If you do not agree with the End User License Contract (EULC), please return the CD and the hardware key immediately back to the Ridom GmbH.

All other applications need to be closed before installing EpiMRSA!

1. Insert the EpiMRSA Program CD into the drive.
   The installation program usually starts automatically, if not, open the CD with the Windows-Explorer and double click the EpiMRSA-3.x.x.exe file.
2. Confirm the on-screen dialog to start the installation.
3. Follow the on-screen instructions until you've completed the installation procedure.
4. The last step of the installation will be the installation of the hardware key driver. The name of the driver is WIBU-Box.
5. Plug in the Ridom hardware key delivered with the CD and wait until Windows has initialized the new USB device.
6. EpiMRSA can now be run by clicking the desktop icon or selecting the entry in the Start Menu.

Installed Components

- Ridom EpiMRSA
- Drivers for Ridom hardware key (WIBU-Box)

Starting EpiMRSA for the First Time

1. Be sure to plug in the Ridom Hardware Key before starting the program.
2. EpiMRSA will first create a profile directory located in your home directory (e.g., using Windows XP this will normally be something like "C:\Documents and settings\<username>\epimrsa"). This directory will contain your configuration file and the error.log file.
3. When the login dialog appears for the first time a message will appear, and EpiMRSA needs to initialize the default database. You can define the path where the database files should be stored, and set the password that is needed to log into the database. By default, the database files will be stored in the profile directory. After the new database is initialized the EpiMRSA session will be started.

   WARNING: The decryption of the database data is only possible using the EpiMRSA password. However, this password itself is not stored within the database and cannot be reproduced or reset when forgotten. It is therefore vital that the password be memorized well or written down. The database cannot be restored without the password!

   For performance reasons, an internal database should always be saved on a local hard disk. If your profile directory is not on the same computer as the EpiMRSA installation, it is recommended to change the path for the database files to a local directory.

Updating the Software

If an update for your EpiMRSA installation is available, an information message will appear on each start of the program (if configured). Using the menu *Help|Software Update|Online Update* an update can be searched and download from the Ridom web-server. The update will be installed after exiting the program.

Note: If you are accessing the Internet through a proxy server, you first need to set the proxy parameters in the EpiMRSA configuration dialog.

If a direct Internet connection is not possible or wished, the update can be downloaded manually from http://www.ridom.de/EpiMRSA/support and installed through the menu *Help|Software Update|Import Update File*.

EpiMRSA Help

- User Guide
  (this document, invoke context-sensitive online-help by pushing the F1-key)
- Quick Reference Card
  (overview of menu, toolbar functions and key shortcuts)
- Help|Info dialog
  (for version and system information)
- Bug Report dialog
  (send feedback messages such as bug reports and feature requests)

Uninstalling EpiMRSA

To remove EpiMRSA from your computer select the Uninstall EpiMRSA icon from the Start Menu. When uninstalling the software, only the application directory will be removed from your system. The profile and the database directory will not be deleted automatically.

If you want to reinstall EpiMRSA, be sure to reboot your computer first. This is strongly recommended to prevent problems with the hardware key driver.

3.Getting Started

Running EpiMRSA

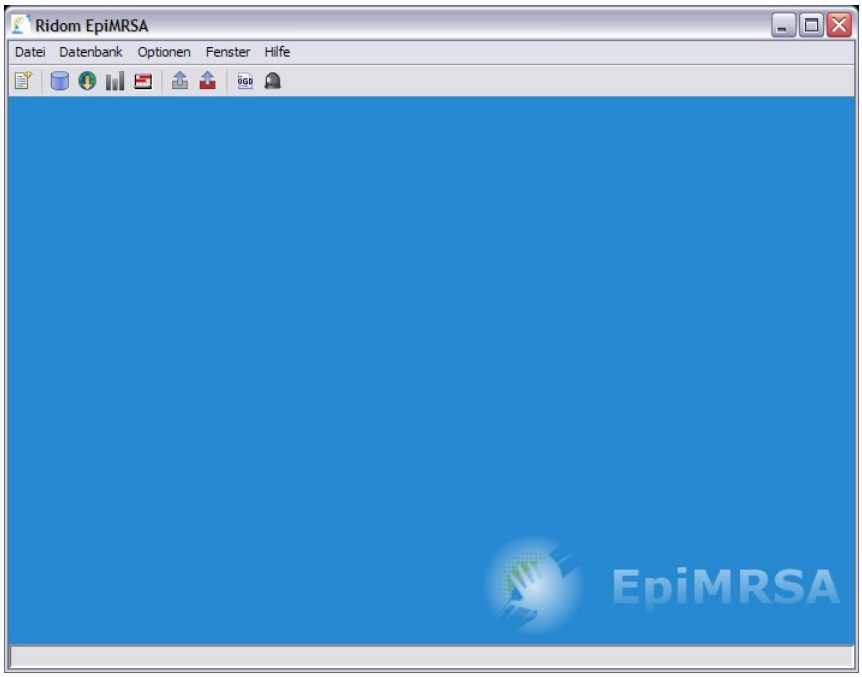
When running EpiMRSA a splash screen appears and after initialization is complete the screen shows a login form you are asked to enter the database password. By default EpiMRSA uses an internal database. If you want to use an external database server, the database configuration can be changed with the manage button.

Using the EpiMRSA Main Window

After entering the correct password and clicking the *Login* button, the main window will appear showing, from top to bottom, the following components:

- Menu bar
- Tool bar
- EpiMRSA desktop
- Status bar

Permanent windows such as those for the Strain Browser are opened inside this main window on the EpiMRSA desktop.

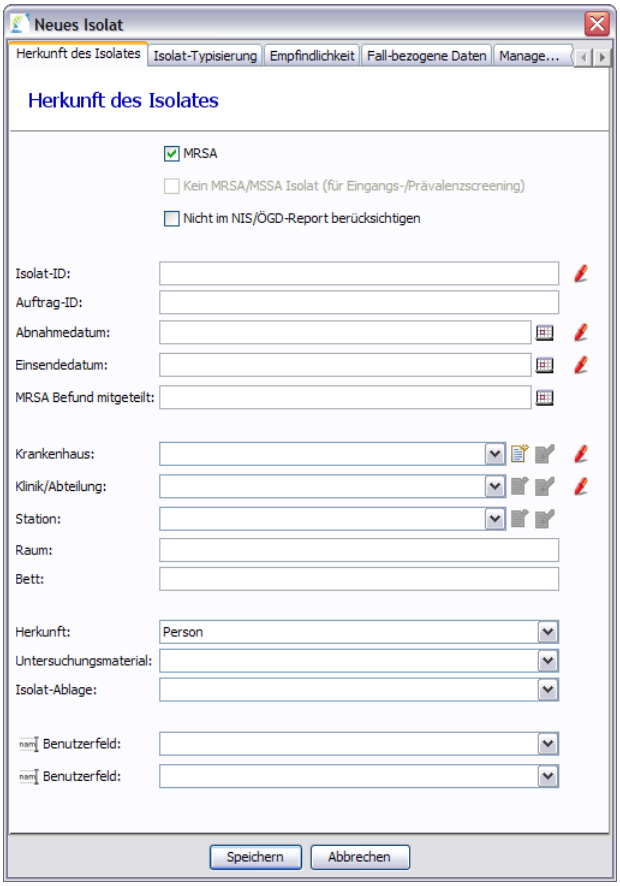


Keyboard Shortcuts

Frequent occurring actions can be conveniently invoked by keyboard shortcuts (e.g. Ctrl-N opens a new entry form). A shortcut is always composed of the key Ctrl and another key. To pop-up right-mouse-button menus.

Entering the Strain Data

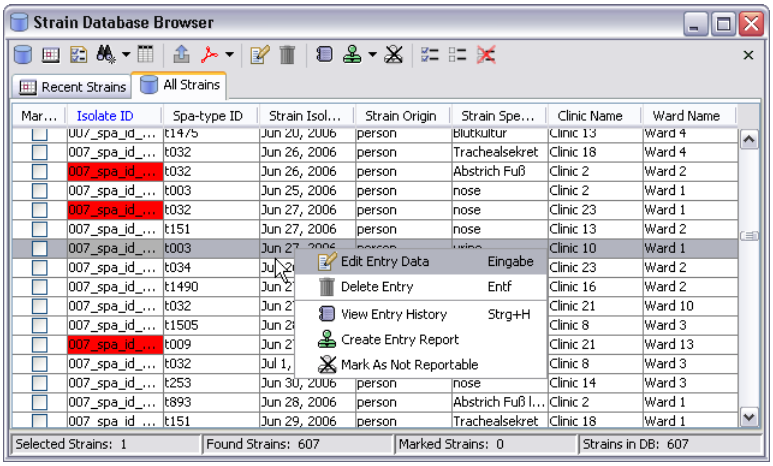
Click on the *New Strain* button to create a new entry in the database. The Entry Data Editor appears containing 7 different tabs for grouping the various classes of information. Be sure to fill in the mandatory fields (Isolate ID, Isolation date, Care unit and Origin) and click the *Save* button. A new strain entry together with the sequences will be created and saved in your database.



Browsing the Strain Data

Click the button in the main toolbar to open the Strain Browser window. When opened it shows initially a list of all entries that were created or edited in the last 30 days ( ). Click the button to search for specific strain entries. A dialog window appears in which search criteria can be defined. The results of the search will be shown as a new tab in the Strain Browser window.

If the Isolate-ID columns is highlighted red, the entry does not contain all data that is necessary for an MRSA-NIS report. Move the mouse over the red marked field to show a tooltip with further details.



Creating Strain Reports

If a strain entry is assigned a spa-type, an entry report can be created. Select the entry in the Strain Browser and click the button to create a report for it. The report can be viewed by opening the entry history with the button.

Retrieving Spa-Types from the SpaServer

When EpiMRSA is started, it automatically checks if your spa-type data is up-to-date by requesting the SpaServer. Click on the button to manually invoke the download of current spa-types and spa-alignment data from the SpaServer.

Note: If you are accessing the Internet through a proxy server, you first need to set the proxy parameters in the EpiMRSA configuration dialog. If you don't have an Internet connection at all, you can receive the up-to-date spa-type information by email.

4.Entering Entry Data

Strain Data Editor

Clicking the *New Strain* button of the main tool bar opens the Strain Data Editor. Since this is an external dialog window there can be only one entry open at any one time. The window shows all the data of an entry organized in 7 different tabs:

- Strain Source (strain/specimen data)
- Strain Type (typing data)
- Susceptibility (susceptibility data)
- Case (person and person-related information)
- Management (isolation management and patient contacts)
- Report (entry report and optional report receiver information)
- Comments (internal and public comment information)

Database entry shortcuts: Ctrl-C and Ctrl-V copies and pastes field content. The right-arrow functions as a quick search for the field content and with the down-arrow you can move in the list of possible field entries.

Strain Source Tab

Defines the strain and specimen data. Mandatory fields are *Laboratory ID*, *Isolation date* (or alternatively *Receipt date*), *Care unit*, *Clinic*, and *Origin*. These mandatory input fields are highlighted until they are filled. If a new strain entry is created from sequence files, the laboratory ID and the isolation date are filled with default values. The default for the laboratory ID is taken from the sequence name and the isolation date default is the last modified date of the sequence file.

Using the User Fields

The last two rows in the Strain Source form are *User Fields*. They have no predefined meaning and can therefore be used for any task or function not covered by the other fields. The label of a user field can be changed and this change will apply to all other entries. Additional user fields are found under the other tabs.

Care Unit, Clinic and Ward Fields

The field *Care Unit* (e.g., a hospital, nursing home or doctor's practice) is a mandatory field for each strain entry. The fields *Clinic* and *Ward* are subunits of the Care Unit and are optional.

A unit (Care Unit, Clinic or Ward) can be selected in the pull-down box or newly created with the button. The button can be used to edit an already existing unit. It should be noted that this will change the data for all strain entries referencing this unit.

The following relationships exist between Care Unit, Clinic and Ward:

- A Care Unit may contain one or more Clinics and one or more Wards.
- A Clinic may have one or more Wards.
- A Clinic can belong to only one Care Unit.
- Each Ward belongs to one Clinic or one Care Unit.

Strain Type Tab

This form is used to gather typing test results for the strains isolated. The first row defines the current spa-type assigned to this strain. If a strain is not typable using *spa* gene sequencing (e.g. when the strain does not harbor the Protein A gene), NT (non-typable) can be selected. The *MRSA / MSSA* field is directly linked to the MRSA check box in the Source tab and to the methicillin row in the Susceptibility tab.

Susceptibility Tab

This tab shows a table in which the susceptibility to various substances can be defined. If the result for *methicillin* is set to “resistant”, the *Penicillin* row is also set to “resistant” automatically.

New substances can be added to the list and will appear in all other strain entries. The user-defined substances can be renamed.

Note: User-defined substances cannot be deleted but are removed automatically if not used in an entry.

Person Tab

The Person tab is only available if the origin of the strain is set to “person”.

The upper part of the form shows input fields for person-related data and person data can be entered in the lower part. The values in these fields are stored encrypted in the database as indicated by the padlock symbol and these fields are NEVER synchronized.

When entering a newly created strain entry or a strain entry for which person data has not yet been entered, the button is selected by default. The person data can be directly entered into the fields and a new person entity will be created for this strain.

When editing a strain entry for which person data has already been entered, the person data fields are shown write-protected. The state of the person data fields can be changed by using the three buttons below:

- The button is used to assign to the strain a person already entered in the database. A search dialog will open in which the search criteria birthday, last name and first name can be entered. A search without any criteria values will display all person entries existing in the database.
- The button disables/enables the write-protection and is therefore used to make the current person data editable. Editing the person data will have an effect on the person data of all strain entries referencing that person.
- The button is used to create a new person entry and to assign it to the strain entry. This will not delete the person entry referenced by the strain previously.

Person entries are automatically deleted when no longer referenced by a strain entry.

Management Tab

This tab can be used to describe the isolation management for this isolate and according information like contact persons of the patient.

Report Tab

This tab is used to customize the external report for this entry. Select the check box *Do not report* if it is planned not to generate a report.

By default the receiver address for an external report is the Care Unit that was assigned to this strain. Alternatively a different receiver address can be entered here.

The text entered into the comment field of the report will be shown in every external report created for this strain. By clicking in this field with the right mouse-key it is possible to insert a time stamp (Ctrl-T) or define (Ctrl-M) and use text macros (Ctrl-1 ... Ctrl-9).

Comments Tab

This tab can be used to enter free text comments. The comment for internal documentation will only appear on internal reports. It will not be shown on external reports and will not be transferred during synchronization. The text entered into the *Report Comment* field will be shown in every external report created for this strain. By clicking in this field with the right mouse-key a time stamp (Ctrl-T) can be inserted or defined (Ctrl-M) and use text macros (Ctrl-1 ... Ctrl-9).

The fields *Public Comment* and *PubMed ID* may be used for descriptions and literature references that should be accessible to all via the SpaServer. Here also it is possible to use macros by clicking in this field (Ctrl-M and Ctrl-1 ... Ctrl-9) with the right mouse-key.

Note: The content of the Public Comment and PubMed ID fields will be transferred during synchronization and will be published on the SpaServer website.

Managing Care Units

Care Units, Clinics and Wards can be created and edited in the Strain Source tab of the Strain Entry Editor. However, there is a specific dialog window providing a convenient way to create, edit and delete these units.

Selecting *Manage Care Units* in the *Database* menu opens a dialog window with three columns the left of which shows all the Care units in the database. Selecting a Care unit in the list shows all Clinics in this Care unit in middle column and/or, in the right column, all Wards associated with it. In the same way, selecting a Clinic shows all Wards in the clinic. The editor for the currently selected units is located at the bottom of each column.

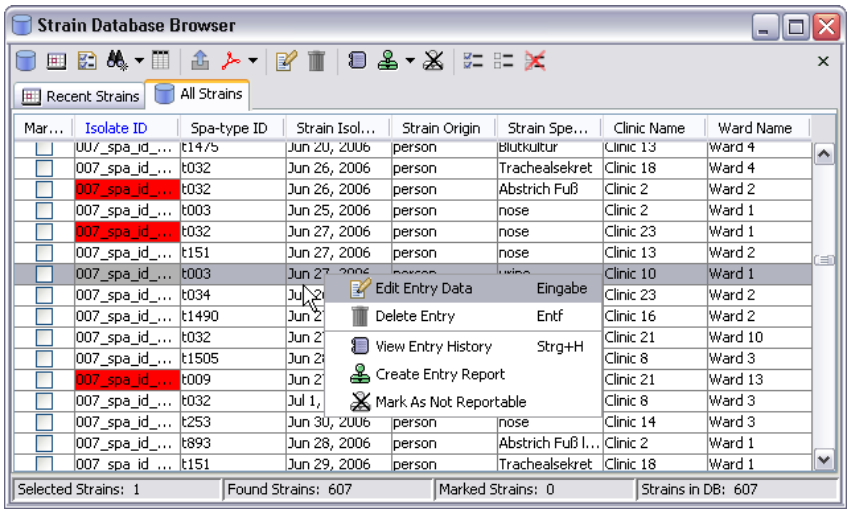
5.Working with the Strain Browser

The Strain Browser Window

Clicking the icon in the main tool bar opens the Strain Database Browser. Since this is an external dialog window, only one window can be opened at any one time. This window contains a tool bar, a tabbed pane and a status bar.

Each tab contains a table in which each row in the table represents one strain entry in the database. The rows can be sorted in ascending or descending order by clicking on the column headers with the left mouse-button. Click on the header with the right mouse-button to hide the column or to add another field to the table.

The first column is always the Isolate-ID. The adjacent columns show other database fields definable by the user. If the Isolate-ID columns is highlighted red, the strain entry does not contain all data that is necessary for an MRSA-NIS report. Move the mouse over the red marked field to show a tooltip with further details.



The first column in each row can be used to ***mark*** the corresponding strain. The marks are kept persistent in the database. They are useful to mark a subset of strains for clustering or exporting.

Use the toolbar buttons

- to mark all or selected strains from the current tab,
- to unmark all or selected strains from the current tab, and
- to unmark all strains in the database.

Searching for Strain Entries

Click the button to define new search criteria. This opens a dialog for selection of the search criteria.

Each row contains a field name, an operator and a value. Additional rows can be added by selecting the *and* checkbox.

The available operators depend on the type of field (i.e. date, number and text). Person data however, are stored encrypted in the database and can only be searched as equal or not equal.

Clicking the *Find* button starts a search and a new tab appears in the Strain Browser showing the strain entries that match the given search criteria.

Clicking on the tab header using the right mouse-key modifies the search criteria or renames the tab.

Note: If the number of strains found in a search is too large for browsing, the table shows only the most recent 2000 entries. The total number of entries found in the search is shown in parenthesis in the status bar. However, exporting from this table (by clicking the button) exports all strain entries. In contrast, the summary report (created by clicking the button) that is created from such a table contains only the strains that were also shown in the table.

Predefined Searches

The tool bar offers shortcuts for often used searches. Clicking on the pull-down arrow of the button shows the list of predefined search criteria:

- Recent Strains: searching all strains which were modified in the last 30 days. To change the length of this time period, right-click on the tab label of a search result table to open its context menu, and use the function *Modify Search.*
- Strains for which no reports were created yet.
- Strains which are currently *marked* by a check in the first column.
- All strains in the database.

Line List

Use the main menu item *Line List* to start a line list search for strains. The search criteria for this search are defined by place, time, case-specifications and spa-types. The last used search criteria are memorized.

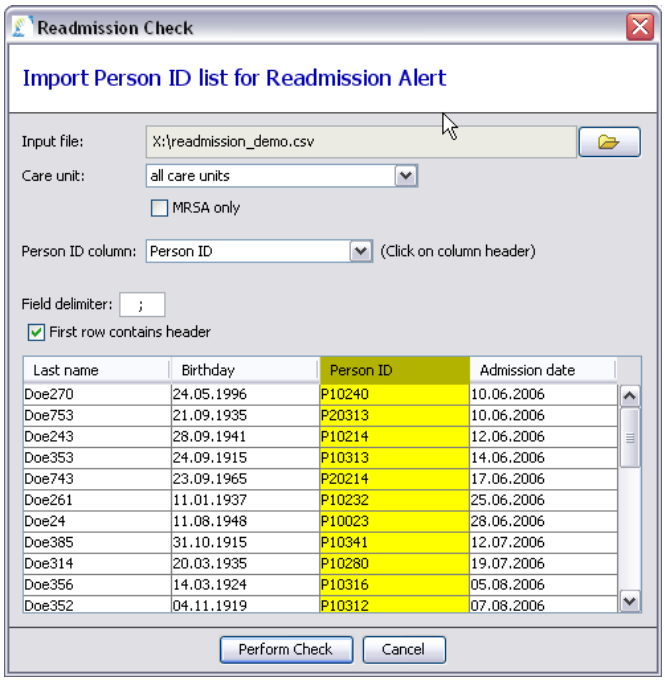
The result of the Line List search is shown in an external dialog window. The data of the found strains can be exported to PDF or into a comma-separated-values file (CSV).

6.Readmission

Readmission Check

This function can be used to detect the readmission of previously colonized or infected patients, by comparing a list of readmissions with the EpiMRSA database. The list must be a CSV (comma separated values) file containing a row per person, e.g. exported from a laboratory information system. It must contain a column with the *Person ID*, and may contain any further columns. In order to compare the list with the database, both must use the same unique keys for the *Person ID* field.

Use the *Tools* menu function *Readmission Check* and open the CSV file. After confirming the file dialog, the data of the CSV file will be shown in the import dialog. Be sure to select the right *Field delimiter* to split the data into the correct number of columns.

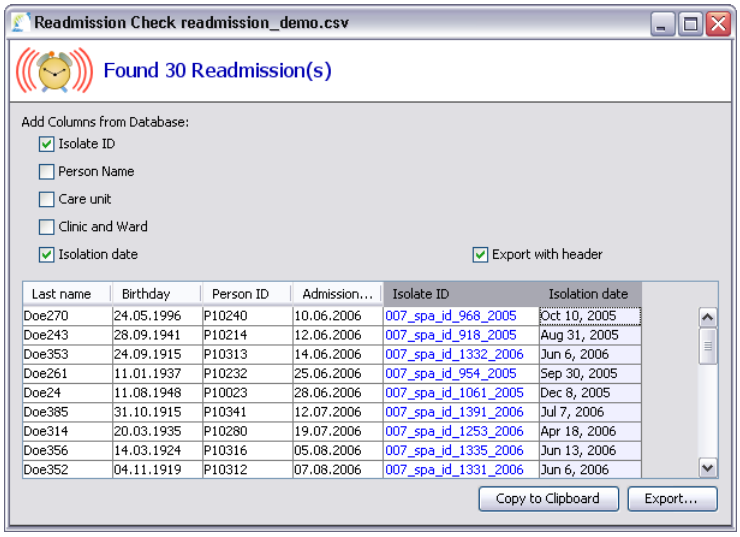


Use the *Care unit* combo box above the table to limit the search to a certain care unit. Select the column that contains the *Person ID*s by clicking on its header or choosing it in the *Person ID*. The selected column will be highlighted yellow.

The settings of *Care unit*, *Person ID column*, *Field delimiter* and *First row contains header* will be memorized when using the Readmission Check function again.

Click on the *Perform Check* button to start the comparing of the *Person ID*s with the entries stored in the EpiMRSA database. If one or more *Person ID*s were found, an alert window appears after the check is completed.

The input rows whose *Person ID*s were found in the database are shown in the result table. The first columns contain the values from the input CSV file. The last column contains the *Laboratory ID*s of all strains that were isolated from the according person. Click on a *Laboratory ID* to open the



corresponding strain data.

Use the check boxes above the result table, to add further columns containing values from the according database strains.

Finally the result table can be exported to a CSV file or copied to the clipboard.

7.Creating Reports

EpiMRSA creates reports in PDF file format and therefore the Adobe Reader needs to be installed in order to view or print these documents.

Strain Table Reports

Clicking the button in the tool bar of the Strain Browser creates a report of the table displayed. This report, due to layout restrictions, contains only the first five columns by default. However, the pull-down menu of the button can be used to change the number of columns displayed or to directly select the report columns required.

Note: Even when more strain entries are found in a search than can be displayed, the report only contains the entries displayed.

Internal and External Strain Entry Reports

If a spa-type is assigned to a strain and the sequence editing is reliable the report for the entry can be created. There are two different types of entry reports, internal and external, to cover different user scenarios. A report is generated by clicking the button and the pull-down menu of the button can be used to configure the report.

Internal Report

This type of report contains nearly all the information stored for an entry. It has a plain table-layout and the internal comment is appended to the report. The internal report is mostly used for communicating results within an institution.

External Report

This document can be used as an official spa-typing report and can be partially customized. The sender of the report and a signature text can be included in the report configuration and this information will appear in all external reports. In addition, a specific report comment and a receiver address can be defined for each entry. Furthermore, a custom logo can be placed in the report (for more details it is referred to chapter 13).

Report History

Every entry report (internal or external) created is stored encrypted in the report archive and is added to the history of the entry report.

Clicking the history button in the Strain Browser tool bar displays the report history for an entry.

The entry history window opens and in the first tab all reports for the selected strain are listed. The windows tool bar provides functions for viewing/printing, exporting and deleting a selected report. A PDF report that is exported can be optionally encrypted by a default or custom password.

Clicking the button marks the report selected as forwarded/sent (this action only sets a marking flag for internal use, however the entry can be no longer be deleted).

MRSA-NIS Report

The MRSA-NIS (Nosocomial Infection Surveillance) report can be used to calculate and report epidemiological data per care unit and year. The fields and the layout of the MRSA-NIS report are based on the German surveillance protocol MRSA-KISS (Krankenhaus-Infektions-Surveillance-System des Nationalen Referenzzentrums für Surveillance von nosokomialen Infektionen, http://www.nrz-hygiene.de/surveillance/mrsa.htm).

The intra-hospital transfers that can be defined in the tab *Management* of the Strain data editor are **not** used in current implementation of the MRSA-NIS report. Each case is always counted for its first clinic/ward (as defined in the tab *Strain Source*).

Care Unit Data (Once per Care Unit)		
Field Name		***Field Value***
Year		*manual input*
Number of *S. aureus* strains	Total	*manual input*
	Infection	*manual input*
	Blood culture	*manual input*
	Case adjusted?	*manual input (yes/no)*
Number of nose swabs	Number	*manual input*
	Per 100 cases	100 * nose swabs / inpatient cases
	Patient adjusted?	*manual input (yes/no)*
Established screening-regime?		*manual input (yes/no)*
Number of beds		*manual input*
Number of ICU-beds		*manual input*
MRSA-rate of all *S. aureus* Isolates (%)		*manual input*

MRSA Cases (Once per NIS-category and once for the care unit as a whole) (NIS-categories: intensive medicine, internal medicine, surgery, other operative discipline, other conservative discipline; not classified Clinics/Wards are listed separately)		
Field Name		***Field Value***
Inpatient MRSA cases		Number of strains with "MRSA/MSSA = **MRSA**" and "Person type = **inpatient**" and if **imported**: "**Admission date** within year" else if **nosocomial**: "**Isolation date** (alternatively **Receipt date**) within year". Special: If a case starts at 31st of December, it is assigned to the following year.
Imported MRSA cases	Colonization	like all cases, but only if "Case type = **imported**" and "Associated with = **colonization**"
	Infection	like all cases, but only if "Case type = **imported**" and "Associated with = **infection**"

Nosocomial MRSA cases	Colonization	like all cases, but only if “Case type = **nosocomial**“ and "Associated with = **colonization**"
	Infection	like all cases, but only if “Case type = **nosocomial**“ and "Associated with = **infection**"
Inpatient MRSA case days		Includes all inpatient MRSA cases that have at least one day within the year, i. e. start date within year or end date within year or start date before year and end date after year. Start date for **imported: Admission date,** for **Nosocomial: Isolation data** (alternatively **Receipt date**). End date: **Discharge date.** Last day a case is not counted (beside 31st of December)
Inpatient MRSA isolation case days		Includes all inpatient MRSA cases that have at least one day within the year, i. e. start date within year or end date within year or start date before and end date after year. Start date: **Isolation start date,** End date: **Isolation end date** (alternatively **Discharge date**). Last day a case is not counted (Number of strains with “MRSA/MSSA = **MRSA**“ and “Person type = **inpatient**" and if **imported**: "**Admission date** within year" else if **nosocomial**: "**Isolation date** (alternatively **Receipt date**) within year". Special: If a case starts at 31st of December, it is assigned to the following year. beside 31st of December)
Inpatient case days		*manual input*
Inpatient cases		*manual input*

MRSA Rates (Once per NIS-category and once for the care unit as a whole)

(NIS-categories: intensive medicine, internal medicine, surgery, other operative discipline, other conservative discipline; not classified Clinics/Wards are listed separately)

Field Name	***Field Value***
Total no. of MRSA cases per 1000 case days	1000 * inpatient MRSA cases / inpatient case days
Total no. of nosocomial MRSA cases per 1000 case days	1000 * nosocomial cases / inpatient case days
Total no. of imported MRSA cases per 100 cases	100 * imported cases / inpatient cases
Total no. of MRSA case days per 100 case days	100 * inpatient MRSA case days / inpatient case days
Total no. of nosocomial MRSA cases per 1000 MRSA case days	1000 * nosocomial cases / inpatient MRSA case days

MRSA Patients (Once per NIS-category and once for the care unit as a whole) (NIS-categories: intensive medicine, internal medicine, surgery, other operative discipline, other conservative discipline; not classified Clinics/Wards are listed separately)		
Field Name		***Field Value***
Inpatient MRSA cases		Number of strains with “MRSA/MSSA = **MRSA**“ and “Person type = **inpatient**" and if **imported**: "**Admission date** within year" else if **nosocomial**: "**Isolation date** (alternatively **Receipt date**) within year". Special: If a case starts at 31st of December, it is assigned to the following year.
MRSA Patients		Number of patients of inpatient MRSA cases. Inpatient MRSA cases without person data are counted as individual patient.
MRSA readmissions		Number of readmitted MRSA cases of MRSA patients.
Additional blocked bed-days		Sum of additional blocked beds of all inpatient MRSA cases.
Decontamination status		Sum of each decontamination status for inpatient MRSA cases.
	not initiated	
	not done	
	aborted	
	unsuccessful	
	provisionally successful	
	successful	
	in progress	

ÖGD Report

The German version of EpiMRSA can create in addition an ÖGD (“Öffentlicher Gesundheitsdienst”) report. This surveillance report was drafted in cooperation with Euregio MRSA-net (http://www.mrsa-net.org) and is also based on the MRSA-KISS protocol (Krankenhaus-Infektions-Surveillance-System des Nationalen Referenzzentrums für Surveillance von nosokomialen Infektionen, http://www.nrz-hygiene.de/surveillance/mrsa.htm).

An explicit description of the ÖGD report is available under the Help menu of the German version of EpiMRSA.

8.Early Warning System

Early Warning System

The Early Warning System (EWS) of EpiMRSA can be used to detect possible MRSA outbreaks in a care unit, clinic or ward. Each time a (newly created or modified) strain is saved to the database the EWS checks for potential outbreaks.

The settings for the EWS can be defined in the EpiMRSA preferences or in the alert overview. The EWS searches for strains, that fulfill the defined criteria, and triggers an alert, if the defined minimum count is reached.

This search is done sequentially finding all strains of a possible outbreak chain with the maximum allowed distance between two consecutive strains. The place for these strains is defined by the selected detection level for this hospital. Hospitals which are not listed in the settings dialog are not checked at all. Each ward can have one or more *functional relations* to other clinics of the same hospital. The functional relations can be defined when editing the data of the ward.

Detection Level	***Possible Outbreak Strains***
Ward	Possible outbreak strains must be in the strain's ward, or in any clinic that is linked with the strain's ward by a functional relation, or in any ward that is linked with the strain's clinic by a functional relation.
Clinic	Possible outbreak strains must be in the strain's clinic, or in any clinic that is linked with a ward of the strain's clinic by a functional relation, or in any clinic that has a ward that is linked with the strain's clinic by a functional relation.
Care unit	Possible outbreak strains must be in the strain's care unit (hospital).

Finally it can be defined if all strains of a possible outbreak must have the same spa-type. If the strains must have the same spa-type then an alternative trigger setting can be defined for local high-frequency spa-types. The defined *minimum frequency* is counted in the specified time interval and care unit as the number of MRSA strains with the specific spa-type in relation to all MRSA strains.

Early Warning Alert

When a strain entry is saved and the Early Warning settings are fulfilled, a new alert is triggered. The oldest strain of the possible outbreak strains is used as index strain and the following strains are defined as secondary strains.

An alert is only triggered, if no other alert already exists that has the same index strain, the same secondary strains and the same trigger settings.

Each triggered alert is automatically stored in the database. Use the menu item *Database|Early Warning System* to view and control the alerts. The icon of the menu item shows if there are new

alerts to clarify.

Early Warning Alert Data	
Timestamp	The date and time when the alert was triggered.
State	The state can be 'to clarify', 'false alert' or 'true alert'. Each new alert has the state 'to clarify', it must be manually set to true or false. If the EWS contains alerts with the state 'to clarify', the EWS menu item shows the red flashing light.
Index strain	The oldest strain that was found in the consecutive possible outbreak strains.
Secondary strains	The strains which follow the index strain in the possible outbreak strains.
No. of strains	The number of index and secondary strains.
Comment	A comment for the alert.

Outbreaks

If an Early Warning Alert seems to be true the user can manually define an outbreak.

Outbreaks are never created automatically they can only be defined by the user.

Outbreak Data	
Timestamp	The date and time when the outbreak was created.
Primary strain	The primary strain of the outbreak. Must be selected by the user.
Index strain	The oldest strain in the consecutive possible outbreak strains. The index strain is taken from the chosen alert when creating an outbreak and can be changed by the user.
Secondary strains	The strains which follow the index strain in the possible outbreak chain. The secondary strains are taken from the chosen alert when creating an outbreak and can be changed by the user.
No. of strains	The number of primary, index and secondary strains.
Comment	A comment for the outbreak.

9.Retrieving Spa-Types from the SpaServer.

Configuring the Connection Parameters

Network Connection

The communication parameters can be set in the Configuration window (Menu: *Options*|*SpaServer Download*|*Connection*). Two options are available when communicating with the Ridom SpaServer (connection dialog):

- **Automatic communication via http**
  This is generally the method of choice when connecting to the server when your computer has a direct connection to the Internet or when you can access WWW-sites through a proxy. The correct SpaServer URL is already predefined. If you need to use a proxy to connect to the Internet it is necessary to set the proxy parameters in the connection configuration (If you do not know these parameters ask your network administrator).
- **Manual communication via file export and email**
  For technical or security reasons this is the method of choice when you are unable to connect to the Internet directly. Register at http://www.ridom.de/epimrsa/spatypes to receive new spa-types by email. This emails will have an attached XML file, which can be imported with the button to update the spa-type data of your local database.

Updates

The automatic checks for available software updates and for new spa-type data when EpiMRSA starts can be activated here.

Receiving Information Messages and Software Updates

On occasion the user will receive an html-message from the server when the spa-type download has been performed. This message may include general information or it may be a link to download an important EpiMRSA software update.

Message Archive

The last 10 SpaServer-messages can be read in the message archive accessible through the menu *Help*|*Message* Archive.

Three types of messages are stored here:

- messages concerning the results of spa-type retrievings
- update messages from the server
- messages containing information from the server
- spa-type group alert messages

10.Database Statistics

Viewing the EpiMRSA Statistics

Click on the button to open an internal window that shows the statistics of your local EpiMRSA database.

This window has four tabs:

Database Statistics	Shows a summary of contents and a table with all spa-types in the database, listed according to their local frequency
Database Spa-types	Shows the repeat successions of all spa-types in the database
Database Repeats	Shows the nucleotide sequences of all repeats in the database
BURP Alignments	Shows the missing spa-type alignments, which have to be downloaded (global spa-types) or calculated (local spa-types)

Note: The four documents can be saved as HTML or converted to PDF.

Viewing the SpaServer Statistics

If the network connection was configured for use of the http-protocol, it is possible to retrieve the current content summary of the SpaServer. To display the summary of all spa-types and repeats in an internal window select *View SpaServer Statistics* in the Database menu. This page can be saved locally as HTML. If synchronization by email was chosen, it is necessary to direct the WWW browser to the URL http://www.ridom.de/spaserver in order to view the most recent SpaServer statistics.

11.Database Backup and Data Import/Export

Backing Up the Database

Select *Make Database Backup* in the File menu to create a copy of the local EpiMRSA database for safekeeping. The backup is stored as a zip-archive file.

Importing a Database Backup

Select *Import Backup File* in the File menu to import a saved backup. Importing a backup will completely overwrite the current databases. Therefore you are asked to create a backup of the current data before importing a backup.

Note: Changing the database password has no effect on older backups. Therefore, after importing a database backup, you need to enter the password that was used when the backup file was created!

Checking the Integrity of the Database

Select *Check Database Integrity* in the Database menu to test the database. This test checks for empty datasets, unreferenced foreign keys and illegal repeat sequences. This feature should normally return a “no problems found” message.

Exporting Data

EpiMRSA can export strain entries into comma-separated values (CSV) files. This commonly used file format can be imported by most spreadsheet applications. There are two ways to invoke the CSV export:

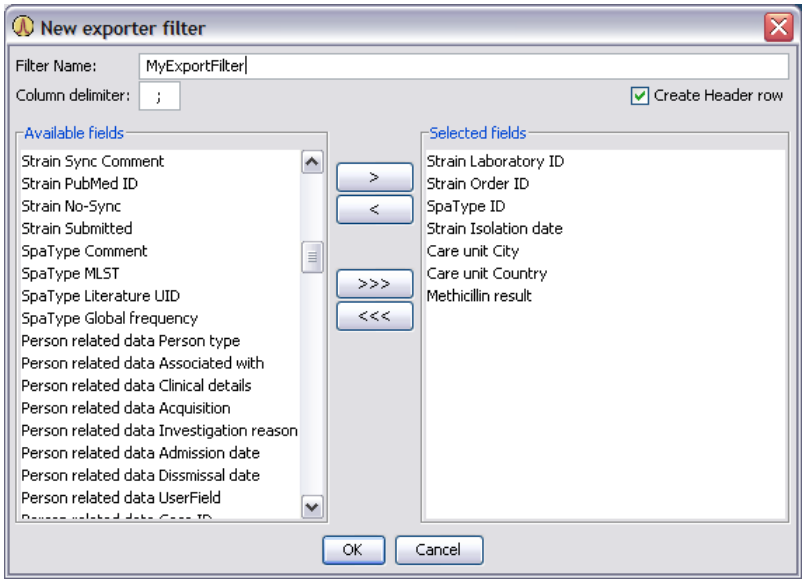
- Select *Export Database Content* in the File menu to export **all** entries (the main tool bar button has the same function), or
- click the button in the Strain Browser tool bar or Linie List result to export the entries that are found in the currently selected search result tab.

When starting the export procedure a file dialog with a Filter pane is opened in which an *export filters* must be chosen or newly created. The export filter defines:

- the data fields that will be exported (sequence data cannot be exported)
- the delimiter for the fields (normally use ',' or ';')
- if a header line with the field names should also be exported

If the export procedure is called in the Strain Browser or the Line List result, then the currently shown table columns are use as the default export filter.

To create a new export filter, click the button to display the Export Filter editor dialog. Then move field labels from the two lists: Available fields and Selected fields. The two upper buttons or a double mouse click moves the label selected whereas the two lower buttons move the complete list. The selected fields list defines the columns exported and their order in the CSV file.



Importing CSV Files

EpiMRSA can import entries from a comma-separated values (CSV) file.

Select the CSV file to be imported from the File menu opened with the *Import Data File* button . The file will be read and then a preview dialog is opened. To import data entries, you need to configure an import filter that maps the columns of the file to database fields. To define a new filter for an input data style:

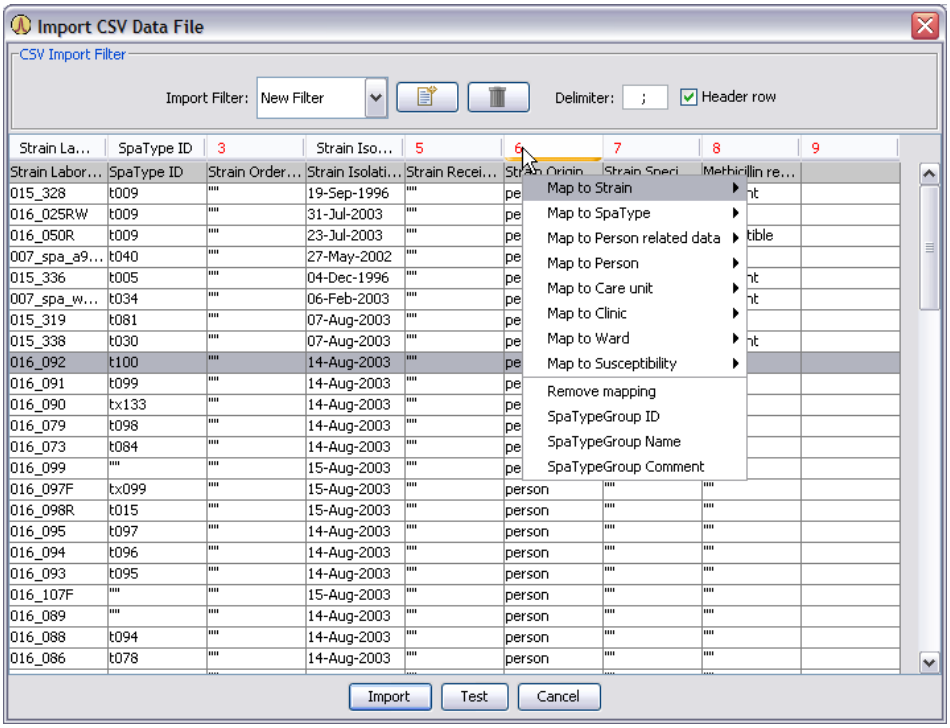
1. Click the button to create a new import filter
2. Choose a descriptive name for this import filter
3. Set the correct delimiter so that all columns appear in the preview
4. Mark the Header row checkbox if the files contain a column name header
5. Map each column to be imported to a database field. To do this, click on the column header using the right mouse-key and choose the field from the pop-up menu. The red column number will be replaced by the field name.

If all columns to be imported are mapped to a database field, click on the *Test* button to check if the actual data can be imported without problems with the previously defined filter. This test will check:

- that each database field is mapped to one column only. The only exception is the Strain Internal Comment field. This field can be used to collect data from several columns not otherwise mapped to a specific database field,
- that the mandatory database fields (Isolate ID, Isolation date, Care Unit name, city and country) are mapped to columns and that these columns contain data in all rows,
- that person data imported include information for the mandatory fields (First name, Last name and Date of Birth),

- that each Laboratory ID in the file is unique and does not already exist in the database,
- that the date conforms to the format: “dd.MM.yyyy” (e.g. 24.09.2003), and
- that the susceptibility results are given in one of the following three forms:

not done	*(empty)*	*(empty)*
resistant	R	-
intermediate	I	+/-
susceptible	S	+



To resolve any problems detected the cells in the table can be edited manually. If the test runs successfully the actual import of the data is achieved with a click on the *Import* button.

12.Configuring EpiMRSA

EpiMRSA Preferences

Select *Preferences* in the Option menu to display the configuration dialog. In the left pane of the dialog, are shown the main groupings: *Appearance*, *SpaServer Download*, *Reports*, *Security*, *External Applications and Advanced* . If one of these main groupings is opened, browsing down to an entry will show the appropriate form of this configuration property in the right panel.

Configuring Appearance

The Colors, Fonts and the Look & Feel of the application can be defined here. The Live window dragging should be disabled on slow systems to prevent redrawing when moving the internal windows. The Localization options can be set to define the date format for displays and reports and the printer page format.

Configuring SpaServer Download

This grouping is used to define the connection parameters and the automatic search for spa-types and software updates. Further details can be found in chapter 9.

Configuring Reports

Entry Report

- Enable/disable the option if a report created is always to be printed.
- Sets a default PDF encryption password for exporting a report.
- Sets the report style:

  internal: contains most fields of an entry; this style is normally used for internal communication within an institution,

  external: creates a report that presents the spa-typing result in an improved and tidier style suitable for external communication purposes.

External Entry Report

External reports can be configured with the following

- The *Design template* defines the layouts of the report. It can be chosen from the available predefined layouts. Further customized design templates can be ordered at support@ridom.de
- The *Logo image* is shown on the header of the report. The given image must be a JPG, PNG or GIF file.
- The *Report sender address* is printed on the right of the page header.
- The *Signature* can be used to print name at the bottom of the report for a possible handwritten signature.

Summary Report

Defines the default number of columns that are to be written to a summary report created from the Strain Browser. Because of restrictions in the layout, more than six columns are not recommended.

PDF Viewer

EpiMRSA requires the Adobe Reader software to be installed in order to display and print the PDF report files. The path to the executable Adobe Reader software should, in most cases, be filled in here automatically. If this is not the case, the user must enter the path here to view and print PDF files.

Configuring Security

Can be used to enable an inactivity lock: If the program window stays inactive (no mouse or keyboard action) for a specified period of time, the program is locked until the login password is entered. The program can also be locked manually by selecting *Lock Program* in the *Options* menu.

External Applications

When using BURP Clustering, EpiMRSA can call the external applications MEGA and SplitsTree if they are installed on the computer. The paths for these application is normally found automatically, but they can be changed here.

Advanced

Memory Usage

Define the maximum memory (RAM) that may be used for EpiMRSA can be configured here. For large databases it is recommended to increase this value depending on the available memory on your computer.

Default Field Values

Define default values for newly created isolates.

Early Warning System

Define the settings for the early warning system.

Noskomial/Imported Cases

Define the expected distance between admission and isolaion date for nosocomial/imported cases

Expert Mode

Can be enabled to show the features of the tool menu (e.g., BURP cluster algorithms).

BURP

Disable auomatic initialising of BURP functions (if Expert Mode is enabled)

Changing Password

To change the database password, select *Change Password* in the Option menu. Note that this process may take some time because, in the case of many stored reports, all the PDF files must be encrypted with the new password.

13.BURP Clustering

These features are only available if the Expert Mode is selected in configuration!

Introduction

This chapter describes the basic principles of the BURP ***(Based Upon Repeat Patterns)*** algorithm for spa-type aligning and clustering and its usage within the software.

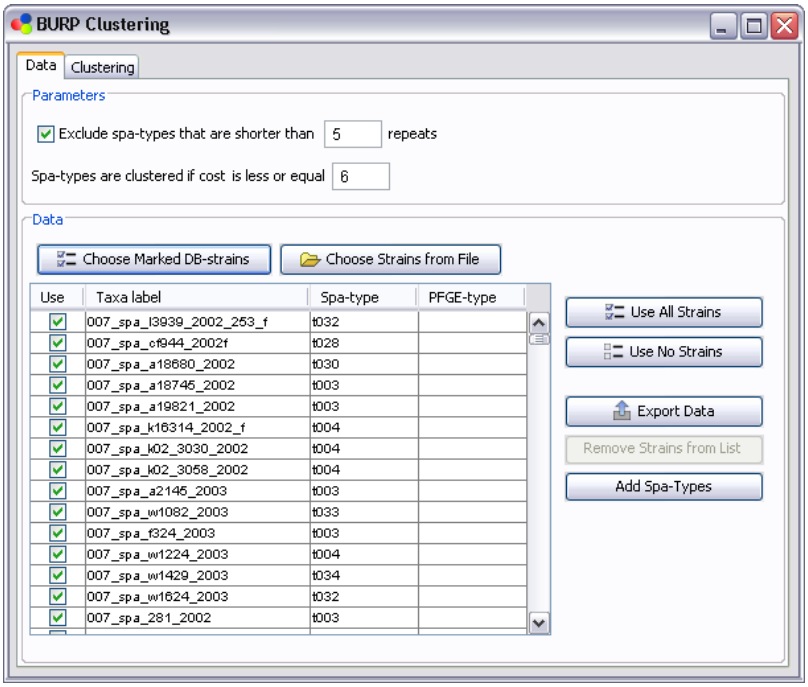
For a detailed description of the ESDI *spa*-type alignment, see: *Sammeth, M., Weniger, T., Harmsen, D and Stoye, J.. Alignment of tandem repeats with excision, duplication, substitution and indels (edsi). in R. Casadio and G. Myers (Eds.): WABI 2005, LNBI 3692, pp. 276–290.*

When starting EpiMRSA, the spa-type alignments must be loaded before the BURP functions can be used. This initialization process is shown by a small dialog window in the lower right corner of the main window and normally takes a few seconds. The spa-type alignments for global spa-types are calculated on the SpaServer after a new spa-type was submitted. They can be downloaded automatically using the normal synchronization process.

Spa-type alignments for local spa-types must be calculated locally. This calculation process starts automatically when a new local spa-type is saved to the database. The calculation of local spa-types can be enabled in the preferences dialog and is disabled by default.

BURP Clustering

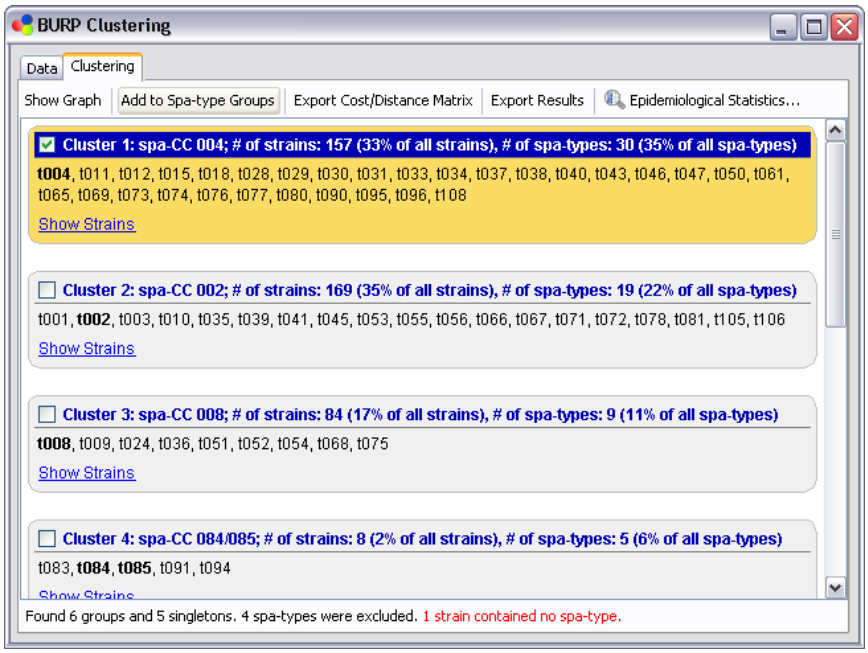
Press the button in the toolbar of the main window, or select *BURP Clustering* in the *Tools* menu to open the BURP dialog window for clustering strains. There are two ways to choose the strain data:



Use the button *Choose Marked DB-strains* to select all marked strains in the database (strains can

be marked in the StrainBrowser). Additionally six data fields of the strain entries can be included: MLST-, PFGE-, SCCmec-, coa-, phage-type, and the user field in the strain type section.

Alternatively use the button *Choose Strains from File* to import the strain data from a CSV-file (comma separated values) containing taxa labels, spa-types, and optionally other fields. An import dialog shows a preview of the imported data. Be sure to set the correct field delimiter (normally ';' or ','). Click on the header of the columns, to customize the mapping of the imported data.

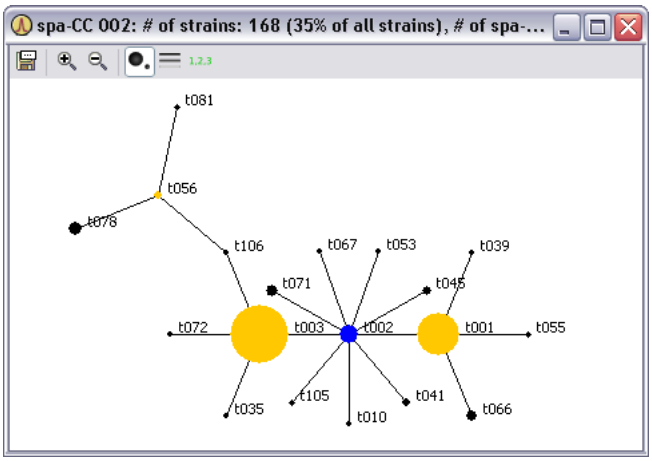

BURP Clustering
Data
Clustering
Show Graph
Add to Spa-type Groups
Export Cost/Distance Matrix
Export Results
Epidemiological Statistics...
Cluster 1: spa-CC 004; # of strains: 157 (33% of all strains), # of spa-types: 30 (35% of all spa-types)
t004, t011, t012, t015, t018, t028, t029, t030, t031, t033, t034, t037, t038, t040, t043, t046, t047, t050, t061, t065, t069, t073, t074, t076, t077, t080, t090, t095, t096, t108
Show Strains
Cluster 2: spa-CC 002; # of strains: 169 (35% of all strains), # of spa-types: 19 (22% of all spa-types)
t001, t002, t003, t010, t035, t039, t041, t045, t053, t055, t056, t066, t067, t071, t072, t078, t081, t105, t106
Show Strains
Cluster 3: spa-CC 008; # of strains: 84 (17% of all strains), # of spa-types: 9 (11% of all spa-types)
t008, t009, t024, t036, t051, t052, t054, t068, t075
Show Strains
Cluster 4: spa-CC 084/085; # of strains: 8 (2% of all strains), # of spa-types: 5 (6% of all spa-types)
t083, t084, t085, t091, t094
Found 6 groups and 5 singletons. 4 spa-types were excluded. 1 strain contained no spa-type.

When the strain data was selected and is shown in the table, click on the *Clustering* tab to perform the clustering. The algorithm tries to find clusters of spa-types so that every spa-type in a cluster is related to at least one other spa-type in the cluster. Each spa-type is member of one cluster only. Spa-types that cannot be assigned to a cluster are kept as *singletons*.

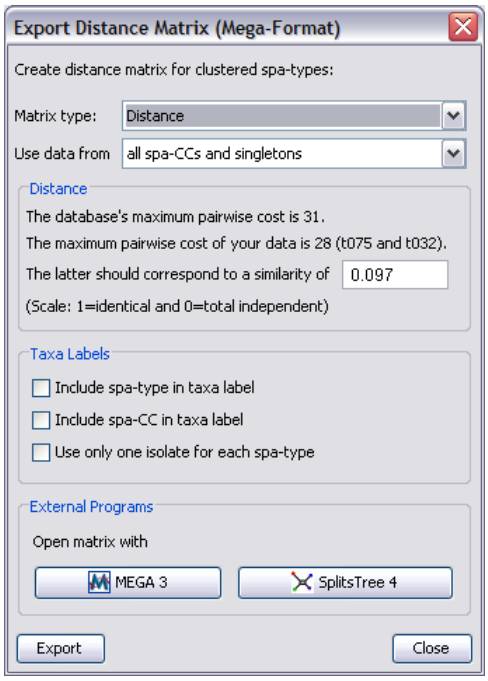
Two clustering parameters can be configured in the Data tab dialog:

- "Exclude spa-types that are shorter than **x** repeats". Because it is impossible to infer the evolutionary history from very "short" spa-types it is recommended to use here a value of at least 4 (default value is 5).
- "Spa-types are clustered if cost is less or equal x". Defines the dimension of clusters. If a greater value is chosen the clusters are going to be bigger and a less number of clusters will be formed (default value is 6).

Use the button *Show Graph* to calculate the BURP graph(s) for the selected cluster(s). BURP graphs are an eBURST-like (Feil et al., 2004) graphical representation of the relation between spa-types. The *founder* of each cluster is colored blue, *subfounders* are colored yellow. If the **visualize strain count** button is selected, the size of the spa-type node represents the number of clustered strains which belong to this spa-type. The actual costs between different spa-types can be visualized by using the other two buttons. The graph can be moved by clicking and dragging with the mouse and it can be zoomed using the mouse wheel. The graph can be saved in various formats. The "gif" format is the recommended bitmap format. If you plan to further edit the graph, the vector-graphic format "svg" is recommended (e.g. use the freeware editor *Inkscape* for further processing).



Use the button *Export Cost/Distance Matrix* to translate and export the distances of the strains in the selected cluster(s) for the use in phylogeny software. If the software *MEGA 3.x* or *SplitsTree 4.x* are installed on your computer, you can use the buttons in this dialog to the start these programs with the selected matrix as input data.



Use the button *Epidemiological Statistics* to perform some statistics on th clustered data (see chapter 8 for details).

Convert Nomenclature

Use the *Convert Nomenclature...* function to convert a repeat succession from Ridom to Kreiswirth nomenclature and vice versa.

Repeat Motif Search

Use the *Repeat Motif Search...* menu entry to find substrings in the repeat successions of known spa-types. The search supports both, Ridom and Kreiswirth, nomenclatures. Additionally the search term may contain standard regular expressions. For a more detailed description of using regular expressions, see appendix F.

Spa-type and Repeat Alignments

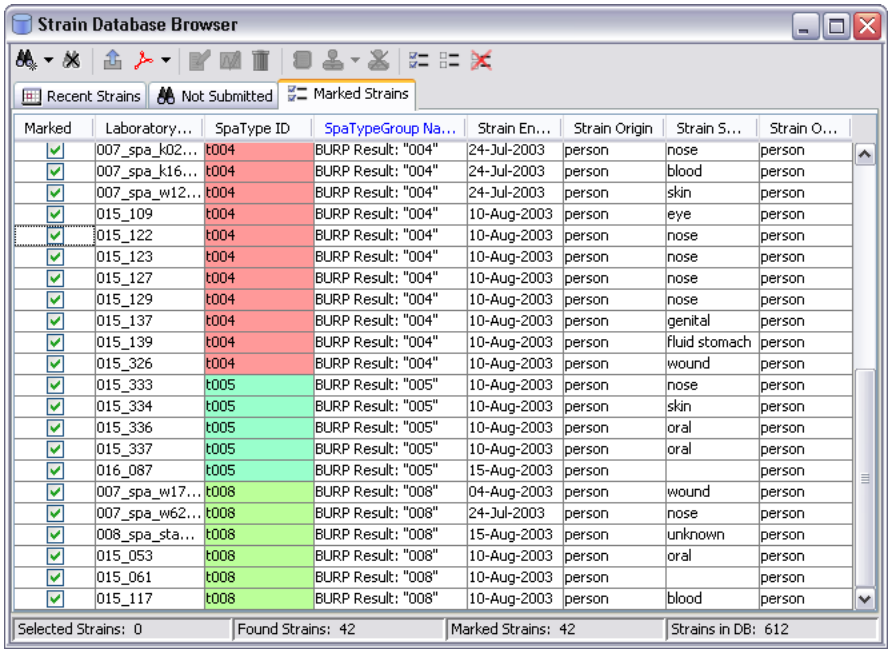
Use *Tools* menu functions *Spa-type Alignment*, *Repeat Alignment* and *Related Spa-types* to examine the alignment or the relation between specific spa-types explicitly.

Spa-type Groups

Spa-types can be arranged in spa-type groups. These groups are only locally defined; they are not synchronized and are only meant for local usage. Each spa-type may belong to one group only. Spa-type groups are conceptually independent of the spa-type clusters, but the BURP Clustering dialog can be used, to add the spa-types of one or more clusters into a spa-type group. Select *Spa-type Groups* from the *Tools* menu, to manage defined groups, create new groups, and edit the following group settings:

Name	A descriptive name for the group
Comment	Any comment
Alert	Define, if an alert should be given, if a new strain with a spa-type of this group appears. The alert can also be defined by a maximum spa-alignment distance to any spa-type of this group. If an alert is triggered a warning message appears
Spa-types	Can be used to add or remove spa-types manually
Color	Defines the background color for all spa-type ID of this group in the Strain Browser

If a spa-type is grouped, the *Strain Database Browser* shows the color of according group in the spa-type column:



Marked	Laboratory...	SpaType ID	SpaTypeGroup Na...	Strain En...	Strain Origin	Strain S...	Strain O...
☑	007_spa_k02...	t004	BURP Result: "004"	24-Jul-2003	person	nose	person
☑	007_spa_k16...	t004	BURP Result: "004"	24-Jul-2003	person	blood	person
☑	007_spa_w12...	t004	BURP Result: "004"	24-Jul-2003	person	skin	person
☑	015_109	t004	BURP Result: "004"	10-Aug-2003	person	eye	person
☑	015_122	t004	BURP Result: "004"	10-Aug-2003	person	nose	person
☑	015_123	t004	BURP Result: "004"	10-Aug-2003	person	nose	person
☑	015_127	t004	BURP Result: "004"	10-Aug-2003	person	nose	person
☑	015_129	t004	BURP Result: "004"	10-Aug-2003	person	nose	person
☑	015_137	t004	BURP Result: "004"	10-Aug-2003	person	genital	person
☑	015_139	t004	BURP Result: "004"	10-Aug-2003	person	fluid stomach	person
☑	015_326	t004	BURP Result: "004"	10-Aug-2003	person	wound	person
☑	015_333	t005	BURP Result: "005"	10-Aug-2003	person	nose	person
☑	015_334	t005	BURP Result: "005"	10-Aug-2003	person	skin	person
☑	015_336	t005	BURP Result: "005"	10-Aug-2003	person	oral	person
☑	015_337	t005	BURP Result: "005"	10-Aug-2003	person	oral	person
☑	016_087	t005	BURP Result: "005"	15-Aug-2003	person		person
☑	007_spa_w17...	t008	BURP Result: "008"	04-Aug-2003	person	wound	person
☑	007_spa_w62...	t008	BURP Result: "008"	24-Jul-2003	person	nose	person
☑	008_spa_sta...	t008	BURP Result: "008"	15-Aug-2003	person	unknown	person
☑	015_053	t008	BURP Result: "008"	10-Aug-2003	person	oral	person
☑	015_061	t008	BURP Result: "008"	10-Aug-2003	person		person
☑	015_117	t008	BURP Result: "008"	10-Aug-2003	person	blood	person

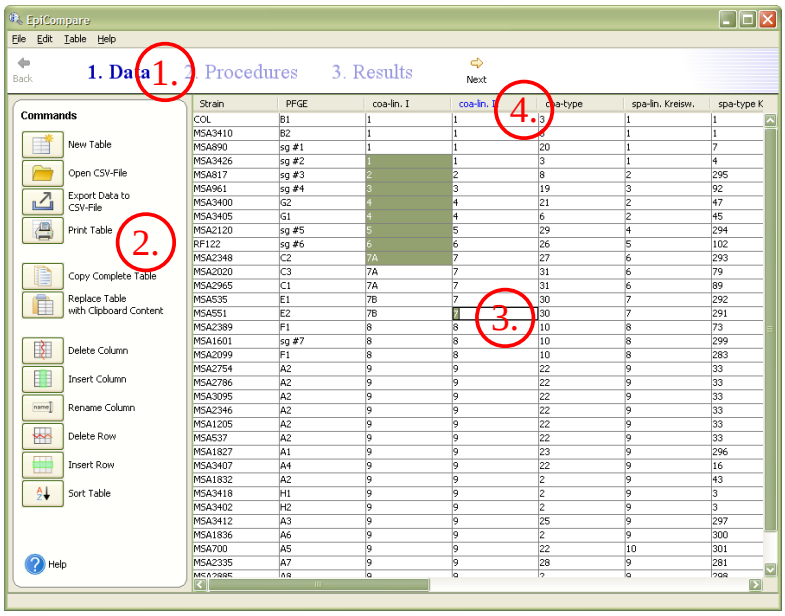
14.Epidemiological Statistics

These features are only available if the Expert Mode is selected in configuration!

Introduction

Epidemiological typing has many different applications. Those include surveillance of infectious diseases, outbreak control and others. Often two ore more different typing methods are available. There are several criteria for evaluating the power of typing methods and for comparing different methods. The underlying mathematical formulas are often quite simple, but the handling of the data can get demanding for large data sets.

The Epidemiological Statics tool can calculate various criteria for data of different typing techniques. It combines easy calculation with ease of data handling.



Data View. The buttons for switching views are below the menu bar (1). The command pane (2) offers the currently available commands. The currently edited cell is indicated (3). A blue table head, as shown in (4), marks the currently sorted column.

Switching Views

The panel below the menu bar is used for switching different views. There are three views: *Data*, which contains a table for the used data, *Procedures*, which allows selection of calculation procedures and *Results*, where the calculation results are displayed. Click on the text in the panel or use the *Back* and *Forward* buttons to switch the views.

Import Data from a CSV-File

Use the button in the command pane to open a CSV-file. Several import-options can be set for CSV-files:

- whether the CSV-file contains a header in the first line or not,
- the delimiter can be set. In most cases this will be “;” or “,”. Take a look at the preview-table to find out if the delimiter is chosen correctly, and
- each column in the table needs an unique name. Columns that have a name assigned are displayed in white. If a column has no name assigned, it is displayed in a light red colour. Click on a column and select a name in the context menu. You can specify a name by selecting the pop-up menu entry *Enter Column Name...* .

Import Data from Clipboard

It is also possible to import a table from the clipboard. This feature supports Microsoft Excel clipboard format. This means that you can select a table (or parts of it) in Excel, copy it to the clipboard and paste it into the program. Press the button to replace the table with the current clipboard content. You will be asked if the first row should be used for selecting column names. If this applies and two or more columns have the same name, numbers are attached to the names to make them unique.

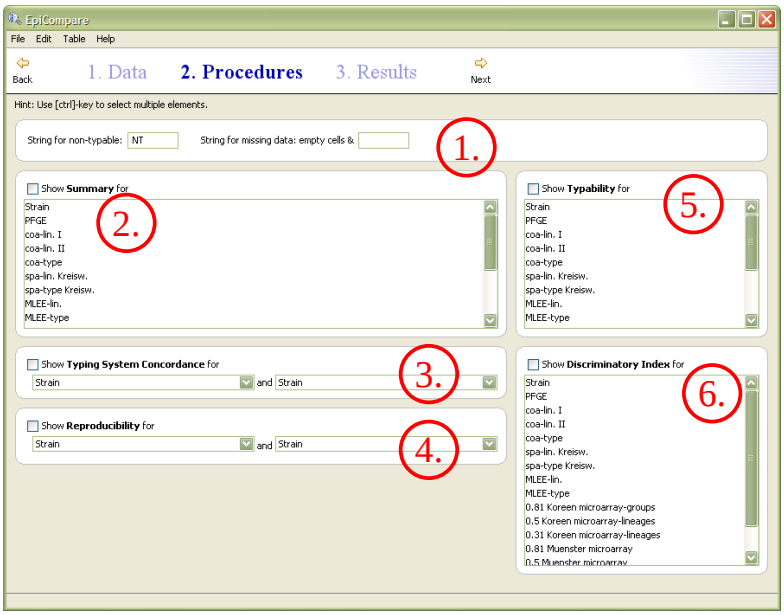
Data View

Each row contains one isolate, and each column contains a specific attribute. The attribute names are unique, this means that two columns cannot have the same name. The table columns can be reordered by dragging them with the left mouse button. Table columns can be selected by clicking their column-head. Multiple columns can be selected by pressing the Ctrl-key while clicking the column-head.
To edit the table, double-click a cell. The Tab-key can be used to traverse the table's cells while editing. The *Table* menu contains functions for modifying and sorting of the table. It is also possible to sort the table by double clicking a column head with the left mouse button. The head of the sorted column appears blue.
It is possible to merge two or more columns with the *Merge Columns* button. A new column is created with a name made out of the names of the merged columns and the new column is filled with the concatenated values of these columns. Be careful with cells containing non-typable values. Check that the merged cells contain the correct data for your usage!

Procedures Selection View

The figure below shows the view that is used for selecting the procedures. See next chapter for calculation details. The panels allows the input of “values” for missing or not non-typable values. The default for missing is an empty text, the default for non-typable values is “NT”. Change this if your dataset uses other “values”.

It is possible to select multiple lines in the lists by using the Ctrl-key while clicking with the mouse-button. Typing system concordance and reproducibility can only be calculated for 2 attributes at once.



Procedures View. The upper panel (1) contains the text for non-typable and missing isolates. Selecting attributes in (2) displays a summary statistic for this attribute. Select (3) – (6) for calculation of: (3) Typing System Concordance, (4) Reproducibility, (5) Typability and (6) Discriminatory Index.

Results View

The results view displays the calculation results of the selected procedures. References for the different procedures are given.

The results can be saved and printed. In addition, they can also be exported to the clipboard and used in word- processor programs, like Microsoft Word.

Calculation Details

Typability

The typability is the proportion of strains that are assigned a type by the typing system. The formula reads:

$$T = \frac{N_t}{N}$$

with:

N_t : the number of isolates assigned a type and N : the number of isolates tested.

The *Epidemiological Statistics* tool uses:
N = Number of isolates that are not missing.
N_t = Number of isolates that are not missing and are typable.

See [Hunter, Gaston 1988], [Struelens, 1996].

Reproducibility

Reproducibility is the ability of a typing system to assign the same type to a strain tested on independent, separate assays. The formula reads:

$$R = \frac{N_r}{N}$$

with

N_r the number of isolates assigned the same type on repeat testing and

N : the number of isolates tested.

The *Epidemiological Statistics* tool uses: the following data:

N = Number of isolates that are not missing (N includes non-typable values).

N_r = Number of isolates that are not missing and have the same value. The value is the same if both isolates are non-typable.

See [Hunter, Gaston 1988], [Struelens, 1996].

Discriminatory Index

Discriminatory index is calculated with the following formula:

$$D = 1 - \frac{1}{N(N-1)} \sum_{j=1}^{s} n_j (n_j - 1)$$

where

N is the total number of strains in the sample population, s is the total number of types described, and n_j is the number of strains belonging to the *j*th type.

A 95% Confidence Interval (*CI*) can be calculated for *D* with the following formula:

$$CI = [D - 2\sqrt{(\sigma^2)}, D + 2\sqrt{(\sigma^2)}] \text{ with } \sigma^2 = \frac{4}{N}\left[\sum \pi_j^3 - (\sum \pi_j^2)^2\right] \text{ and } \pi_j = \frac{n_j}{N}.$$

The *Epidemiological Statistics* tool uses all isolates that have no missing data and are typable for calculation of discriminatory index and 95% confidence interval. Isolates with missing data or isolates that are non-typable are ignored in this calculation.

See [Simpson, 1949], [Hunter, Gaston 1988], [Grundmann et. al. 2001].

Typing System Concordance

Use typing system concordance to compare the results of different typing systems. For calculation, pairs $(x, y): x, y \in Isolates$ of all isolates are created. All pairs are arranged in a 2x2 table, according to their type in both typing systems:

	***System 1,* +**	***System 1,* -**
***System 2,* +**	**A**: # of pairs (x,y) for which x and y have the same type in System 1 and in System 2	**B**: # of pairs (x,y) for which x and y have the same type in System 2 and a different type in System 1
***System 2,* -**	**C**: # of pairs (x,y) for which x and y have the same type in System 1 and a different type in System 2	**D**: # of pairs (x,y) for which x and y have a different type in System 1 and in System 2

The ratio $C_{TS} = \frac{(A+D)}{\text{Total Sum}}$ is the Typing System Concordance.

See [Robinson et. al., 1998].

References

Hunter, P.R., and Gaston, M.A. 1988. Numerical index of the discriminatory ability of typing systems: an application of Simpson's index of diversity, J. Clin. Microbiol. **26:**2465–2466.

Struelens M.J. 1996. Consensus guidelines for appropriate use and evaluation of microbial epidemiologic typing systems, Clin. Microbiol. Infect. **2:**2-11.

Simpson, E.H. 1949. Measurement of diversity, Nature **163:**688.

Grundmann, H., Hori, S., and Tanner, G. 2001. Determining confidence intervals when measuring genetic diversity and the discriminatory abilities of typing methods for microorganisms, J. Clin. Microbiol., **39:**4190-4192.

Robinson, D.A., Hollingshead, S.K., Musser, J.M., Parkinson, A.J., Briles, D.E., and Crain, M.J. 1998. The IS1167 insertion sequence is a phylogenetically informative marker among isolates of serotype 6B *Streptococcus pneumoniae*, J. Mol. Evol. **47:**222-229.

C.Regular Expressions

Using Regular Expressions in Repeat Motif Search

Use the repeat motif search to find substrings in the repeat successions of the known spa-types. The search supports both, Ridom and Kreiswirth nomenclature. Additionally the search term may contain standard regular expressions.

Examples:

- **?** matches the preceding expression or the null string
  (e.g.: "G**B?**G" matches "GG", and "G**B**G")
- ***** matches the null string or any number of repetitions of the preceding expression
  (e.g.: "G**B***G" matches "GG", "G**B**G", "G**BB**G", "G**BBB**G", and so on)
- **+** matches one or more repetitions of the preceding expression
  (e.g.: "G**B**+G" matches "G**B**G", "G**BB**G", "G**BBB**G", and so on)
- **( )** can be used for grouping several characters in combination with the operators above
  (e.g.: "12**(-34)?**-12**"** matches "12-12" and "12-**34**-12")
- ***{m,n}*** matches between *m* and *n* repetitions of the preceding group
  (e.g.: "12**(-34){2,3}**-12" matches "12-**34**-**34**-12" and "12-**34**-**34**-**34**-12")

D.EpiMRSA Version History

- Ridom EpiMRSA version 3.0, released March 2011
  (revised version for further networks)
- Euregio EpiMRSA version 2.0, released June 2010
  (improved support for Windows 7)
- Euregio EpiMRSA version 1.1, released March 2007
  (introduced the NIS/ÖDG-Reports and the Early Warning System)
- Euregio EpiMRSA version 1.0, released November 2006
  (first release of the software)

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